



Appendix B

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7. A method for expressing a transgene in a skeletal muscle cell, comprising the step of introducing into the cell a recombinant adeno-associated virus (rAAV) comprising a transgene operably linked to sequences which control its expression, wherein the rAAV is at least as free of contamination with a helper virus as is obtained by subjecting the rAAV to four rounds of cesium chloride gradient centrifugation and wherein the transgene is expressed in the cell.

8. The method according to claim 7, wherein the transgene encodes a secretable protein.

9. The method according to claim 8, wherein the protein is selected from the group consisting of Factor IX, β -interferon, insulin, erythropoietin, growth hormone, and parathyroid hormone.

10. The method according to claim 7, wherein the rAAV consists essentially of, from 5' to 3', 5' AAV inverted terminal repeats (ITRs), a heterologous promoter, the transgene, a polyadenylation sequence, and 3' AAV ITRs.

12. A recombinant adeno-associated virus (AAV) comprising sequences encoding factor IX and regulatory control sequences which permit expression of factor IX in a cell, wherein the rAAV is at least as free of adenoviral helper virus as is obtained by subjecting said recombinant AAV to four rounds of cesium chloride gradient centrifugation.

13. A composition comprising a physiologically compatible carrier and a recombinant adeno-associated virus (AAV) comprising sequences encoding factor IX and regulatory control sequences which permit expression of factor IX in a cell, wherein the rAAV is at least as free of adenoviral helper virus as is obtained by

subjecting said recombinant AAV to four rounds of cesium chloride gradient centrifugation.

14. The composition according to claim 13, wherein said composition comprises about 1×10^8 to about 5×10^{11} particles of the recombinant adeno-associated virus.

15. The composition according to claim 14, wherein said composition comprises at least 10^9 particles of the recombinant adeno-associated virus.

16. The composition according to claim 13, wherein the composition comprises 10^{12} to 10^{13} genomes of the recombinant adeno-associated virus per milliliter carrier.

17. The composition according to claim 13, wherein said composition is formulated for intramuscular injection.

18. A method of delivering a transgene to a mammal comprising the step of:

administering intramuscularly to a mammal a composition comprising a biologically compatible carrier and a recombinant adeno-associated virus (rAAV) comprising a transgene encoding a secretable protein operably linked to sequences which control expression thereof, wherein said rAAV is substantially free of contamination with an adenovirus, wherein said rAAV is at least as free of adenoviral helper virus as is obtained by subjecting said recombinant AAV to four rounds of cesium chloride gradient centrifugation, whereby the protein is secreted from rAAV-transduced muscle cells.

19. The method according to claim 18, wherein the composition comprises about 1×10^8 to about 5×10^{11} particles of the rAAV.

20. The method according to claim 18, wherein the composition comprises at least 10^9 particles of the rAAV.

21. The method according to claim 18, wherein the composition comprises 10^{12} to 10^{13} genomes of the rAAV per milliliter carrier.

22. The method according to claim 18, further comprising the step of monitoring expression of the transgene in the mammal.

23. The method according to claim 18, wherein the level of contaminating adenoviral helper virus is the same as that obtained by subjecting said recombinant AAV to four rounds of cesium chloride centrifugation.

24. The composition according to claim 13, wherein the level of contaminating adenoviral helper virus is the same as that obtained by subjecting said recombinant AAV to four rounds of cesium chloride centrifugation.